

FIGURE 1

| mAb | Mean Fluorescence Intensity | | | % Gated |
|------------|-----------------------------|------|-----------|---------|
| | L1.2-CCRS | PBMC | L1.2-CCRS | |
| mouse IgG1 | 10 | 4 | 1 | 1 |
| 2D7 | 75 | 29 | 92 | 36 |
| PA8 | 48 | 9 | 73 | 3 |
| PA9 | 79 | 5 | 96 | 3 |
| PA10 | 80 | 8 | 96 | 5 |
| PA11 | 107 | 8 | 96 | 10 |
| PA12 | 115 | 8 | 96 | 8 |
| PA14 | 81 | 14 | 96 | 22 |

FIGURE 2

| INHIBITOR COMBINATION | CONCENTRATION RATIO | ASSAY | COMBINATION INDEX | |
|-----------------------|---------------------|--------|-------------------|----------------|
| | | | 90% Inhibition | 50% Inhibition |
| PA12:2D7 | 10:1 | Entry | 0.043 | 0.291 |
| | 2:1 | Fusion | 0.017 | 0.019 |
| | 10:1 | Fusion | 0.087 | 0.067 |
| | 50:1 | Fusion | 0.158 | 0.046 |
| PA12:PA14 | 10:1 | Entry | 0.437 | 0.535 |
| | 10:1 | Fusion | 0.22 | 0.263 |
| PA14:2D7 | 1:1 | Entry | 2.85 | 1.85 |
| | 1:1 | Fusion | 1.34 | 1.74 |
| PA12:PA11 | 1:1 | Entry | 0.707 | 0.641 |
| PA12:RANTES | 1000:1 | Fusion | 0.331 | 0.156 |
| | 100:1 | Fusion | 1.6 | 1.37 |
| | 100:1 | Fusion | 0.972 | 0.962 |
| PA12:CD4-IgG2 | 10:1 | Fusion | 0.3 | 0.31 |
| | 1:1 | Fusion | 0.957 | 0.566 |
| | 1:1 | Fusion | 1.127 | 0.302 |

FIGURE 3

| | | IC ₅₀ values (μg/ml) | | | |
|------|----------|---------------------------------|------------------------|--------------------------|-------------------------|
| | Epitopes | cell-cell fusion inhibition | viral entry inhibition | gp120-binding inhibition | calcium flux inhibition |
| PA8 | Nt | - | - | - | - |
| PA9 | Nt/ECL2 | - | - | 0.24 | - |
| PA10 | Nt/ECL2 | - | - | 0.13 | - |
| PA11 | Nt | 25.5 | - | 0.33 | - |
| PA12 | Nt | 10.0 | - | 0.24 | - |
| PA14 | Nt/ECL2 | 1.7 | .024 | 1.58 | 6.4 |
| 2D7 | ECL2 | 1.6 | .026 | 1.38 | 4.5 |

FIGURE 4

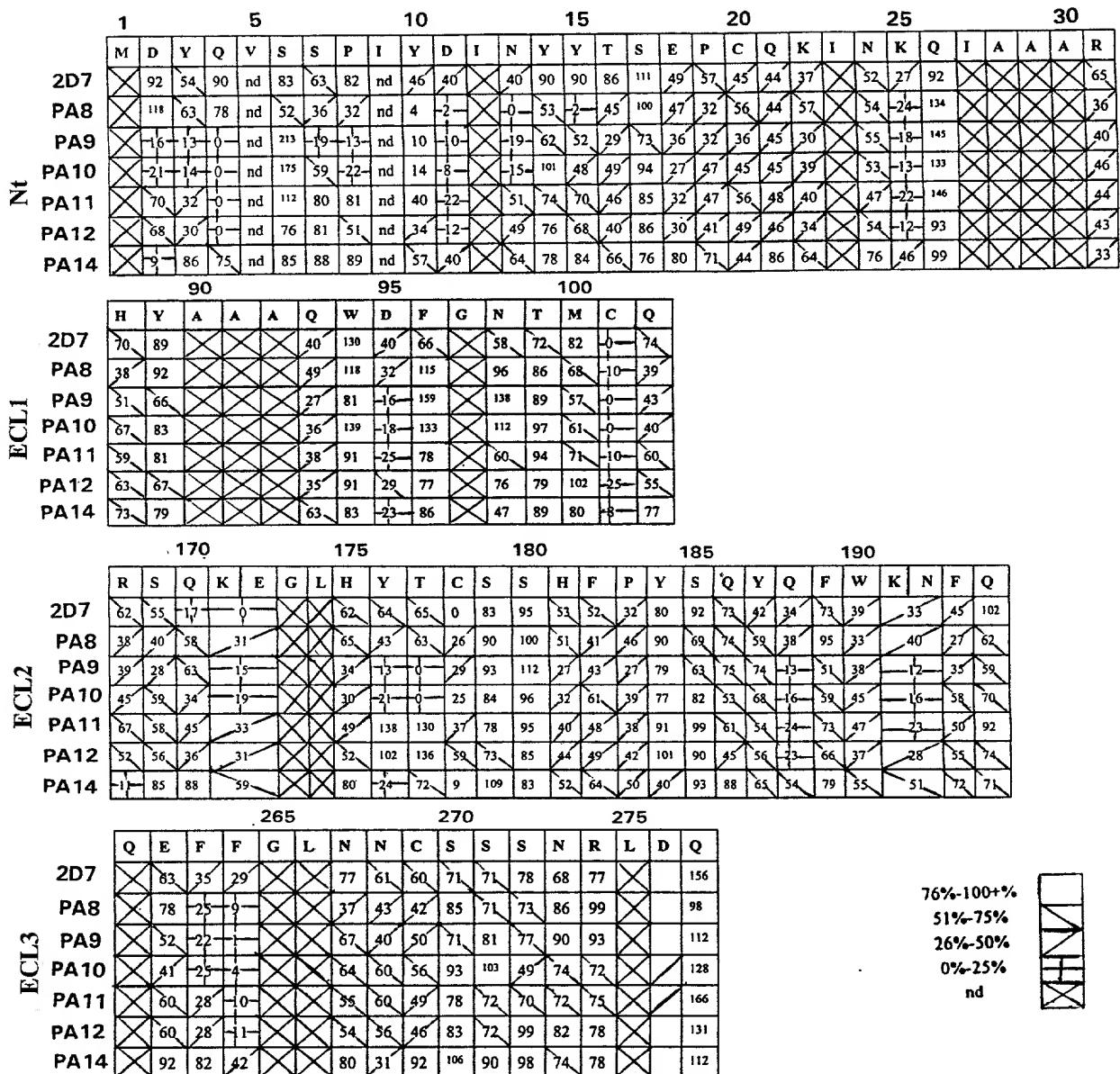


FIGURE 5A

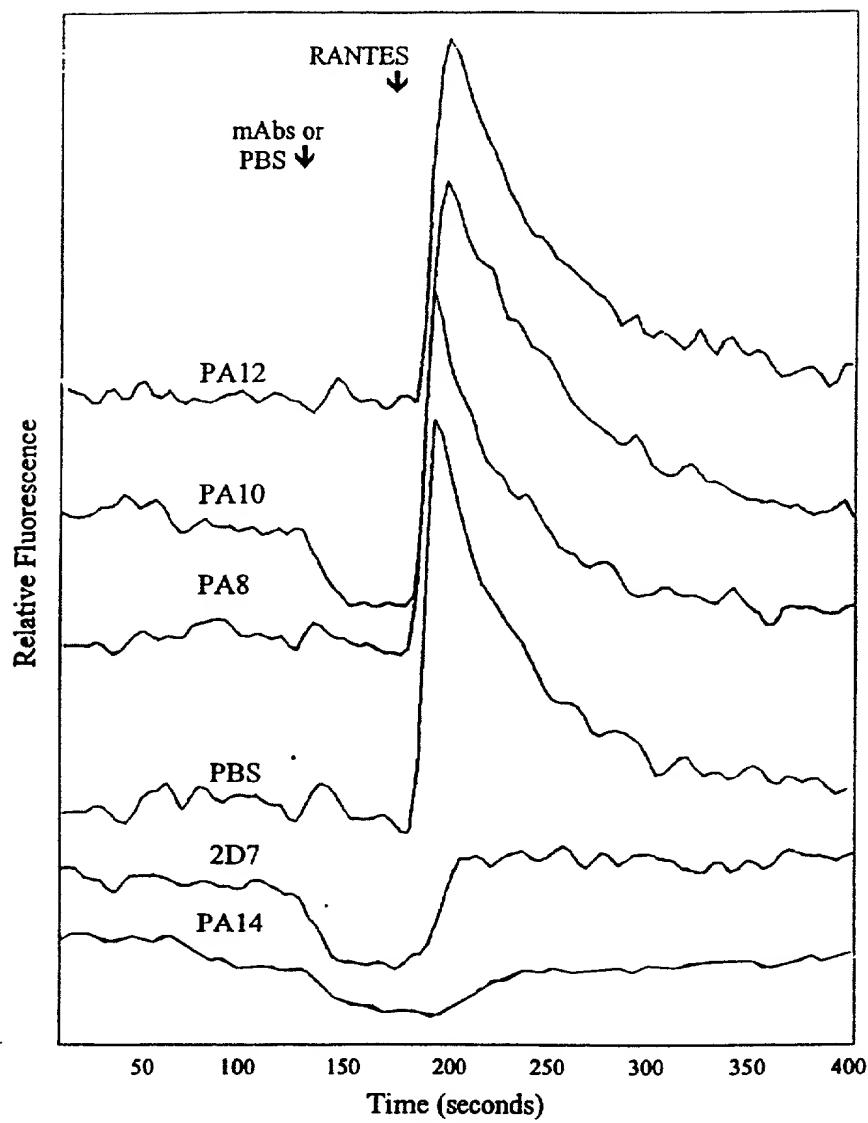


FIGURE 5B

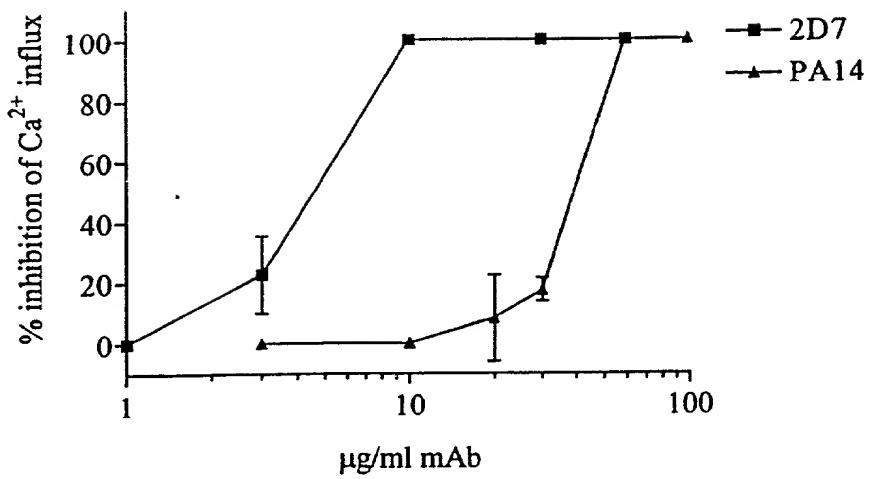


FIGURE 6A

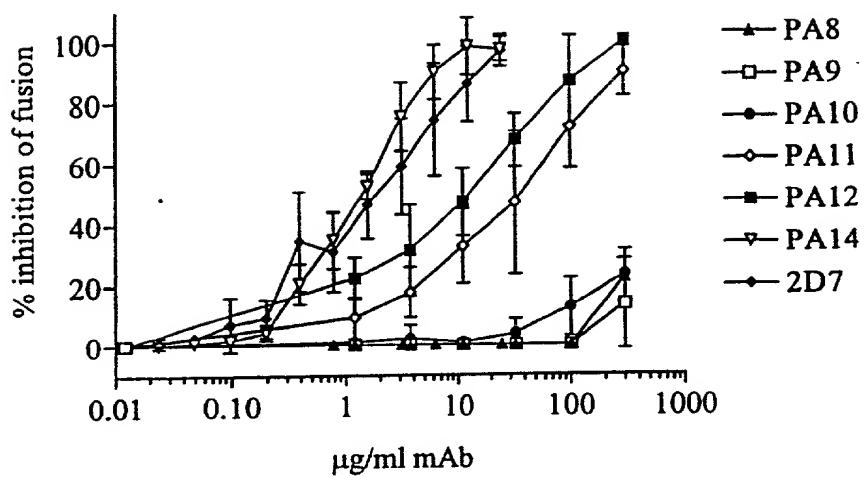


FIGURE 6B

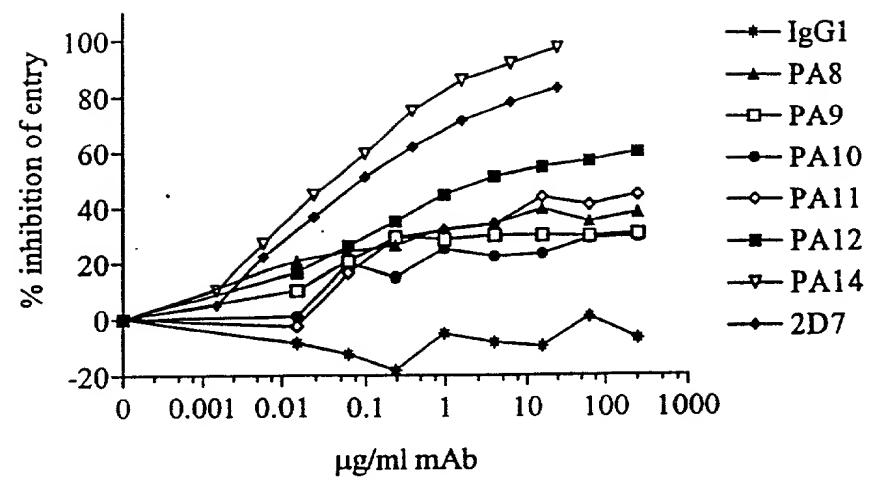


FIGURE 6C

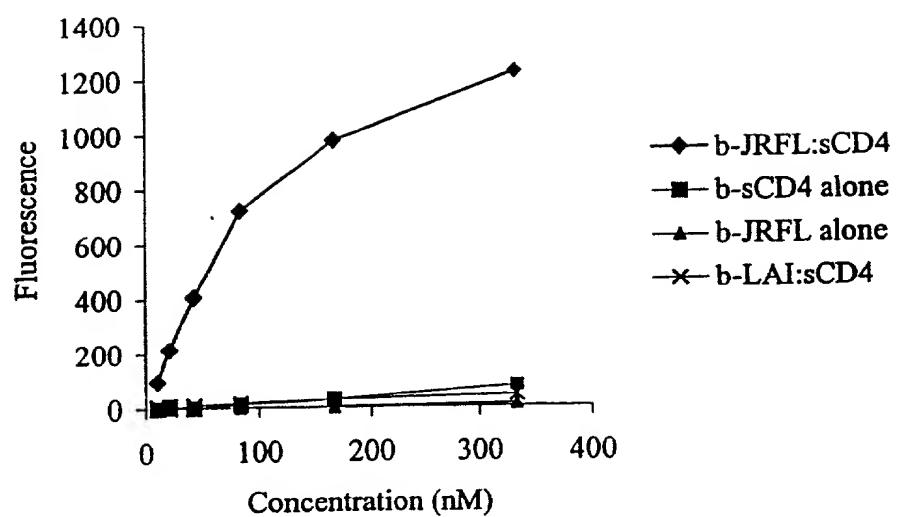


FIGURE 6D

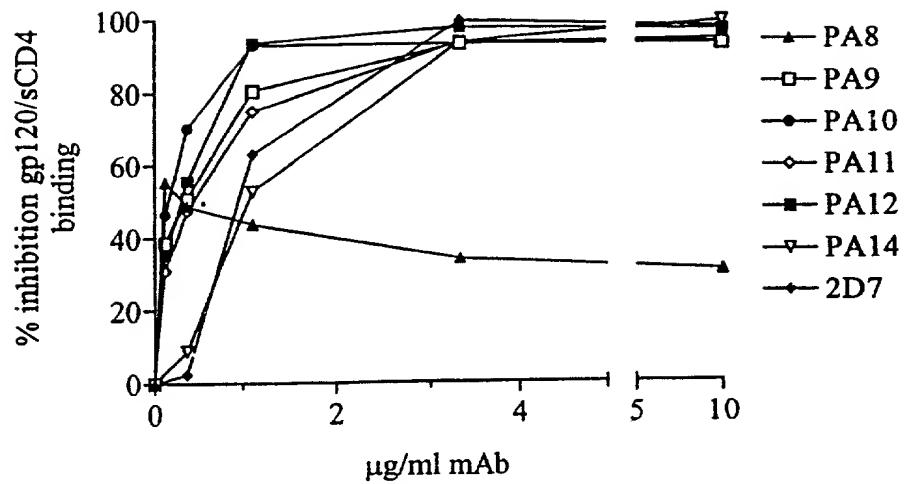
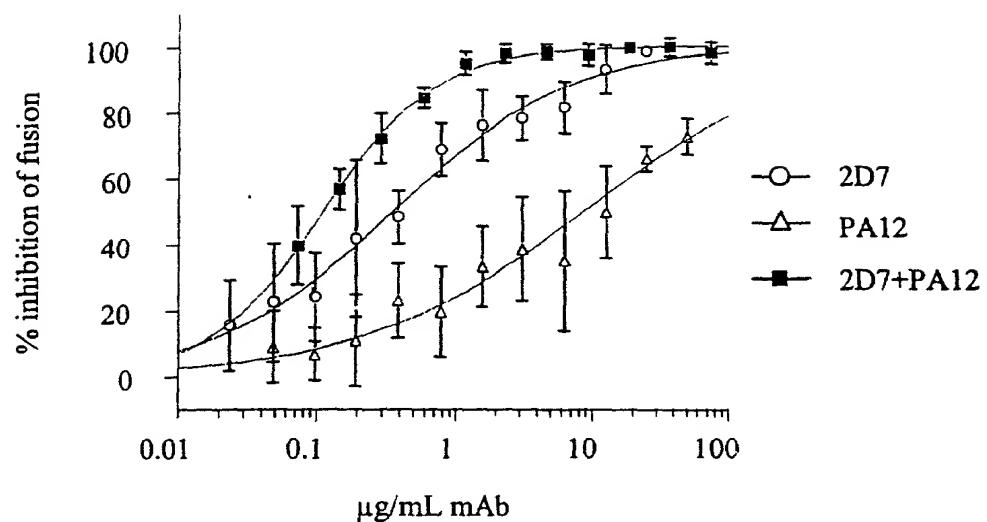


FIGURE 7

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FIGURE 8

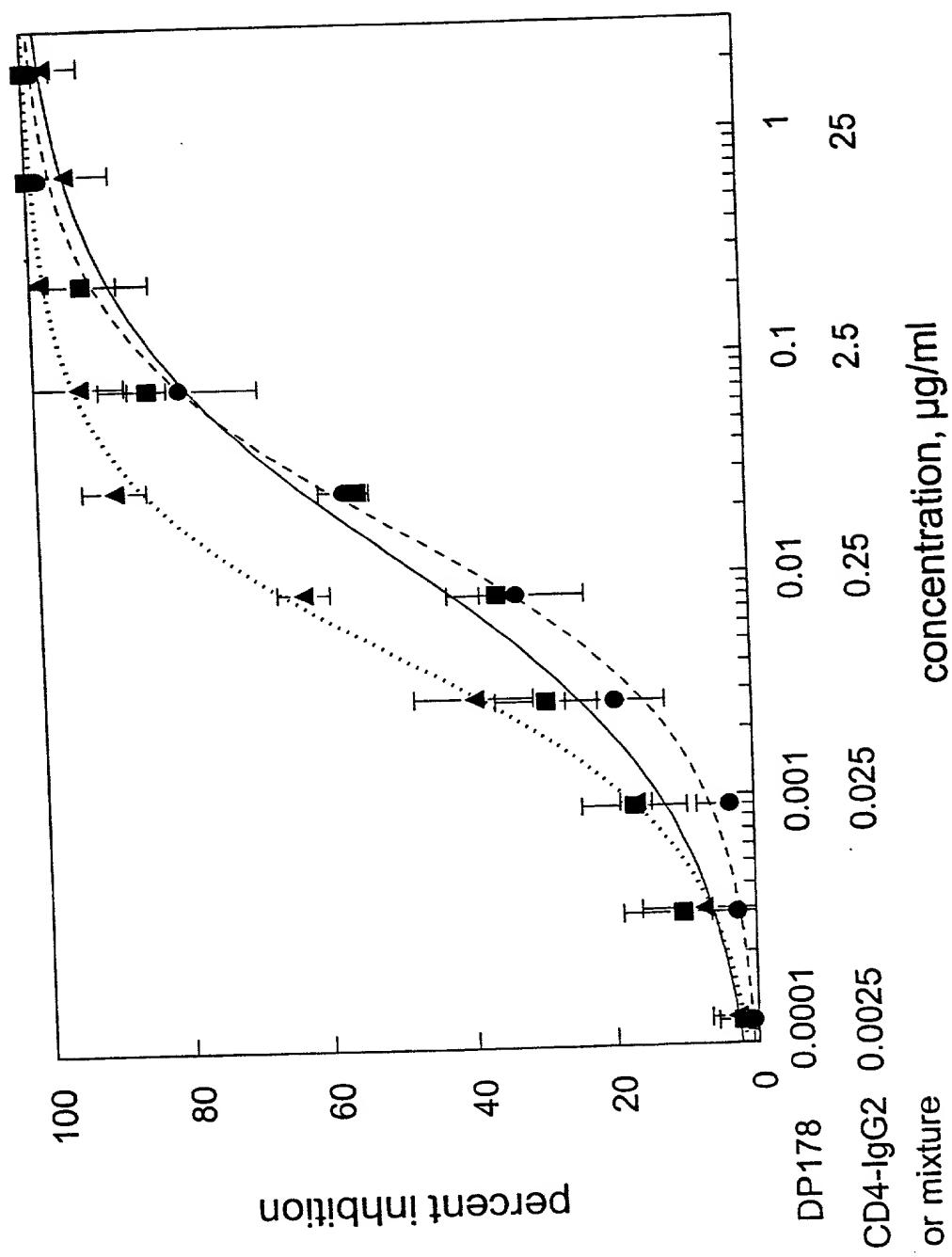


FIGURE 9

| Percent Inhibition | Combination Index | | | |
|-----------------------|--------------------------|----------------|------|------|
| | CD4-IgG2:T-20 Mass Ratio | | | |
| | 25:1 (low) | 25:1 (high) | 5:1 | 1:1 |
| 95 | 0.32 | 0.20 | 0.22 | 0.50 |
| 90 | 0.38 | 0.25 | 0.27 | 0.55 |
| 85 | 0.43 | 0.29 | 0.30 | 0.59 |
| 80 | 0.47 | 0.33 | 0.34 | 0.62 |
| 75 | 0.51 | 0.36 | 0.37 | 0.65 |
| 70 | 0.54 | 0.39 | 0.40 | 0.67 |
| 65 | 0.58 | 0.42 | 0.43 | 0.70 |
| 60 | 0.61 | 0.45 | 0.45 | 0.73 |
| 55 | 0.65 | 0.48 | 0.49 | 0.75 |
| 50 | 0.69 | 0.51 | 0.52 | 0.78 |

FIGURE 10

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| Percent Inhibition | T-20 | | | CD4-IgG2 | | |
|--------------------|---------------------------------|----------------|-------------|---------------------------------|----------------|-------------|
| | Concentration, $\mu\text{g/ml}$ | Dose Reduction | | Concentration, $\mu\text{g/ml}$ | Dose Reduction | |
| | | Alone | Combination | | Alone | Combination |
| 99 | 1.1 | 0.17 | 6.6 | 130 | 4.3 | 29 |
| 95 | 0.21 | 0.044 | 4.9 | 19 | 1.10 | 17 |
| 90 | 0.10 | 0.024 | 4.2 | 7.8 | 0.59 | 13 |
| 70 | 0.025 | 0.0076 | 3.3 | 1.6 | 0.19 | 8.4 |
| 50 | 0.011 | 0.0039 | 2.8 | 0.60 | 0.095 | 6.3 |

FIGURE 11A

| Percent Inhibition Index | PRO 542 | | | PA12 | | | T-20 | | |
|--------------------------|-------------|-------------------|------|----------------|-------------------|------|----------------|-------------------|-----|
| | Combination | Concentration, nM | | Dose Reduction | Concentration, nM | | Dose Reduction | Concentration, nM | |
| | | Alone | Mix | | Alone | Mix | | Alone | Mix |
| 95 | 0.41 | 10 | 2.1 | 4.8 | 730 | 2.8 | 260 | 94 | 19 |
| 90 | 0.45 | 7.0 | 1.6 | 4.4 | 320 | 2.1 | 150 | 63 | 14 |
| 70 | 0.47 | 4.1 | 0.92 | 4.5 | 72 | 1.2 | 60 | 30 | 8.1 |
| 50 | 0.48 | 3.1 | 0.66 | 4.7 | 28 | 0.87 | 32 | 19 | 5.8 |
| | | | | | | | | | 3.3 |

PRO 542, PA12 and T-20 were used in an approximate 1:1:10 molar concentration ratio.

FIGURE 11B

| Percent Inhibition | Combination Index | PRO 542 | | | PRO 140 | | | T-20 | | |
|--------------------|-------------------|-------------------|------|----------------|-------------------|------|----------------|-------------------|-----|----------------|
| | | Concentration, nM | | Dose Reduction | Concentration, nM | | Dose Reduction | Concentration, nM | | Dose Reduction |
| | | Alone | Mix | | Alone | Mix | | Alone | Mix | |
| 95 | 0.40 | 8.5 | 1.9 | 4.5 | 19 | 1.0 | 19 | 140 | 17 | 8.2 |
| 90 | 0.39 | 7.1 | 1.5 | 4.7 | 13 | 0.77 | 17 | 100 | 13 | 7.7 |
| 70 | 0.37 | 5.3 | 0.87 | 6.1 | 7.2 | 0.46 | 16 | 57 | 7.7 | 7.4 |
| 50 | 0.35 | 4.6 | 0.63 | 7.3 | 4.9 | 0.34 | 14 | 40 | 5.6 | 7.1 |

PRO 542, PRO 140 and T-20 were used in an approximate 2:1:20 molar concentration ratio.

FIGURE 11C

| Percent Inhibition | Combination Index | PRO 542 | | | PRO 140 | | | T-20 | | |
|--------------------|-------------------|-------------------|------|----------------|-------------------|-------|----------------|-------------------|-----|----------------|
| | | Concentration, nM | | Dose Reduction | Concentration, nM | | Dose Reduction | Concentration, nM | | Dose Reduction |
| | | Alone | Mix | | Alone | Mix | | Alone | Mix | |
| 95 | 0.24 | 61 | 2.5 | 24 | 11.9 | 0.72 | 17 | 156 | 22 | 7.1 |
| 90 | 0.22 | 32 | 1.4 | 23 | 8.4 | 0.40 | 21 | 96 | 13 | 7.4 |
| 70 | 0.19 | 9.8 | 0.50 | 20 | 4.5 | 0.14 | 32 | 40 | 4.5 | 8.9 |
| 50 | 0.18 | 4.7 | 0.26 | 18 | 3.0 | 0.074 | 41 | 23 | 2.3 | 10 |

PRO 542, PRO 140 and T-20 were used in an approximate 4:1:30 molar concentration ratio.

FIGURE 11D

| Percent Inhibition | Combination Index | PRO 140 | | | T-20 | | |
|--------------------|-------------------|-------------------|------|----------------|-------------------|-----|----------------|
| | | Concentration, nM | | Dose Reduction | Concentration, nM | | Dose Reduction |
| | | Alone | Mix | | Alone | Mix | |
| 95 | 0.56 | 12 | 1.8 | 6.7 | 156 | 55 | 2.8 |
| 90 | 0.55 | 8.4 | 1.1 | 7.4 | 96 | 35 | 2.7 |
| 70 | 0.55 | 4.5 | 0.51 | 8.8 | 40 | 16 | 2.5 |
| 50 | 0.56 | 3.0 | 0.31 | 9.9 | 23 | 10 | 2.4 |

PRO 140 and T-20 were used in an approximate 1:30 molar concentration ratio.

Triple Combination Synergistically Blocks HIV-1 Entry (I)

FIGURE 12

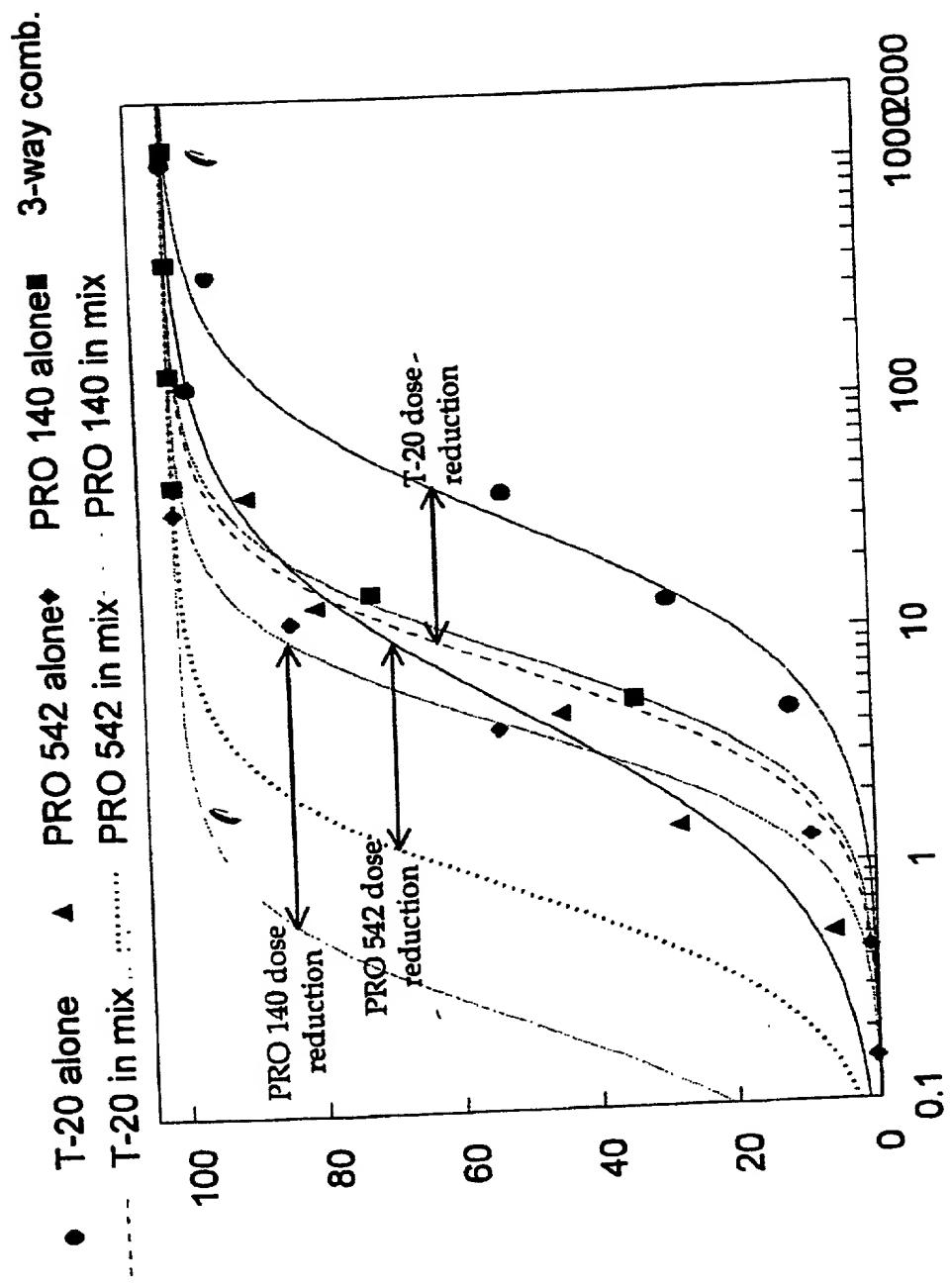


FIGURE 13. *Effect of PA14 and control IgG on HIV-1 RNA levels*